REMARKS/ARGUMENTS

Claims 1-61 are pending in this Application. Claims 6-8 and 15-60 have been cancelled; claims 1, 9 and 61 have been amended; claims 62-72 have been added.

Claims 8 and 15-60 have been withdrawn as being drawn to non-elected inventions, and claims 6-7 as being drawn to non-elected species of elected Group I. Applicants thank the Examiner for considering D1-FRIL from *Dolichos lab lab* and Yam FRIL from *Sphenostylis stenocarpa* as species of the FRIL family (Office Action, page 2, section 2). Please cancel claims 6-8 and 15-60 without prejudice. Claims 6-8 and 15-60, which are being cancelled as being drawn to non-elected inventions, are being cancelled for reasons unrelated to patentability.

The specification has been amended as requested by the Examiner to correct priority, to correct minor typographical errors, and to insert proper reference to trademarks.

Formal drawings are being submitted herewith.

Claims 1 and 9 have been amended to require that each FRIL family member binds to a normally glycosylated FLT3 receptor, and that each FRIL family member preserves progenitor cells. Claim 1 has been additionally amended to require that the FRIL family member isolated from *Dolichos lab lab* includes the sequence TNNVLQXT (SEQ ID NO: 24). Support for these claim amendments can be found in the specification, for example, at page 19, lines 18-24).

Claim 61 has been amended to incorporate the limitation of claim 57. Support for this claim amendment can be found in claim 57 as originally filed.

Claims 62-66, dependent upon claim 9, and claims 67-71, dependent upon claim 61, have been added to further characterize the invention. Support for these new claims can be found throughout the specification, for example, in originally filed claims 2-5.

Claim 72 has been added to cover a pharmaceutical comprising (a) an essentially pure composition of one or more members of the FRIL family of progenitor cell preservation factors wherein each FRIL family member binds to a normally glycosylated FLT3 receptor and wherein each FRIL family member preserves progenitor cells; (b) a chemotherapeutic selected from the group consisting of cytarabine, doxorubicin, and 5-fluorouracil; and (c) a pharmaceutically acceptable carrier. Support for this new claim can be found throughout the specification, for example, at page 36, lines 10-15, and at page 40, lines 15-18.

None of the above amendments to the specification, drawings, or claims adds any new matter to the Application as filed.

Specification

(a) Priority:

The Examiner has inquired whether Applicants desire to obtain the benefit of the filing date of U.S. Patent No. 6,310,195 (Office Action, page 3, section 3). Applicants submit that the instant Application already claims priority to U.S. Application Serial No. 08/881,189, filed June 24, 1997. Applicants have amended the specification to indicate that this prior application has issued as U.S. Patent No. 6,310,195.

(b) Use of Trademarks:

In compliance with the Examiner's instructions (Office Action, page 4, section 6) and to comply with the provisions of MPEP § 608.01(v), the specification has been amended to point out the proprietary nature of the trademark, FICOLL-PAQUE®.

(c) Minor clerical errors:

The Examiner has requested that the specification be checked to correct the presence of possible minor errors (Office Action, page 10, section 16). Applicants have amended the specification to correct all identified minor errors.

It is submitted that no new matter has been added.

Drawings

The Examiner has alleged that the previously submitted formal drawings fail to comply with 37 C.F.R. § 1.84 (Office Action, page 3, section 4). New formal drawings (Figures 1-37) have been submitted herewith that comply with the Official Draftsperson's instructions. Specifically, (i) any erasures, alterations, overwritings, interlineations, folds and copy machine marks in Figure 18 have been removed to comply with 37 C.F.R. § 1.84(e); (ii) views have been labeled separately and properly in Figures 13A-14D and Figures 29A-29E to comply with 37 C.F.R. § 1.84(h); (iii) lines, numbers and letters have been modified to be uniformly thickened and well defined, clean, durable and black in Figures 1-10, 24A, 25-33F and 36A to comply with 37 C.F.R. § 1.84(i); and (iv) numbers and reference characters have been modified to be plain

and legible in Figures 1-10, 16, 22A-D and 25-33F and Figure legends have been modified in Figures 1-10 and 11-14B to comply with 37 C.F.R. § 1.84(p).

Applicants aver that this ground of objection has been overcome and therefore request that this objection be withdrawn.

Request for References

The Examiner has requested that the references filed with an IDS in the prior application U.S. Application Serial No. 08/881,189 be resubmitted, because these citations have been crossed out and the references cited therein cannot be found (Office Action, page 4, section 5). To assist the Examiner, Applicants submit herewith the IDS filed in the prior application U.S. Application Serial No. 08/881,189 along with the references cited therein (Appendix B).

Rejection Under 35 U.S.C.§ 112, Second Paragraph

Claim 61 stands rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite and ambiguous in being dependent upon non-elected claim 57 (Office Action, page 4, section 8).

Claim 61 has been amended to remove reference to non-elected claim 57. Upon entry of the instant amendment, Applicants respectfully aver that this rejection has been rendered moot.

Rejections Under 35 U.S.C.§ 112, First Paragraph

(i) Claims 1-5, 9-14, and 61 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly not reasonably providing enablement for the cited claims. The Office Action states that the specification although the specification is enabling for an essentially pure composition of one or more members of the FRIL family, wherein FRIL is Dl-FRIL, PV-FRIL, or Yam-FRIL, it "does not reasonably provide enablementfor an essentially pure composition of one or more embers of any FRIL family of progenitor cell preservation factors" (Office Action, p. 5, first paragraph).

Applicants respectfully traverse this rejection.

As an initial matter, Applicants respectfully note that since claim 7 has been withdrawn as being drawn to a non-elected invention, this rejection, as it applies to claim 7 (see Office Action, p. 5, first paragraph) is moot.

Moreover, Applicants respectfully aver that the specification enables the invention as claimed in claims 1-5, 9-14, and 61. The instant specification has provided considerable direction and guidance on how to practice the claimed invention and presented sufficient working examples to enable one of ordinary skill in the art to make and use the invention as claimed.

Applicants have clearly defined the characteristics of any proteins that are FRIL family members (see, *e.g.*, page 19, lines 17-26). For further clarification, Applicants have enumerated these limitations in the claims. Specifically, a FRIL family member, as presently claimed, must be able to bind to a normally glycosylated FLT3 receptor, and each FRIL family member must be able to preserve progenitor cells. In their specification, Applicants have provided methods to isolate and purify FRILs (see, *e.g.*, Example 1; Example 5; and Example 22), and the nucleic acid and amino acid sequences of three representative FRILs (see, *e.g.*, pages 55-56; page 83; and pages 120-121). In addition, Applicants have provided detailed guidance for identifying new FRILs (see specification, *e.g.*, at page 50, lines 8 through page 51, line 16), and have provided methods to determine whether an isolated lectin preserves progenitor cells (see, *e.g.*, page 22, line 22 through page 23, line 10).

Applicants posit that their disclosure of numerous FRIL family members, in addition to the description of common characteristics shared by all FRIL family members, is sufficient to enable the ordinarily skilled artisan to practice the invention, as claimed, without undue experimentation. Following the guidance provided by the specification, the ordinarily skilled artisan could easily isolate and identify a lectin as a FRIL family member based on that lectin's ability to bind to a normally glycosylated FLT3 receptor and its ability to preserve progenitor cells.

The Office Action has noted that the *Wands* factors are useful for determining whether undue experimentation is required to practice the invention. These factors include "(1) how much experimentation is necessary, (2) how much direction or guidance is given, (3) whether working examples are provided, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability of the art, and (7) the breadth of the claims," *In re Wands*, 858 F.2d 731, 735 (Fed. Cir. 1988).

Looking to each of the *Wands* factors, Applicants note that although some additional experimentation may be necessary to identify a FRIL family member whose sequence is not

provided in the specification, the Federal Circuit has been clear that just because additional experimentation may be necessary, the additional experimentation is not undue if the specification provides a reasonable amount of guidance (see Johns Hopkins Univ. v. CellPro, Inc., 152 F.3d 1342, 1360 (Fed. Cir. 1998). As discussed above, very detailed guidance *is* provided in the specification to enable the ordinarily skilled artisan to practice the invention. Indeed, the characteristics of FRIL family members which are recited in the claim would clearly inform the routinely skilled artisan whether a lectin is or is not a FRIL family member. Numerous working examples of the purification of FRIL family members are provided in the specification. Moreover, the nature of the invention, namely, a biological molecule that preserves progenitor cells, is very similar to the invention in the *Wands* case—both rely on screening numerous candidates for a biological characteristic. In the *Wands* case, that characteristic was high affinity binding to HbsAg. In the present invention, the characteristics are an ability to bind to a normally glycosylated FLT3 receptor and an ability to preserve progenitor cells. As in the *Wands* case, the present invention resides in a field of art, namely molecular and cellular biology, that is relatively predictable, that typically engages in routine experimentation, and one in which the relative skill of the ordinarily skilled artisan is very high. Moreover, the prior art of the present invention describes the isolation and screening of lectins for biological activity (see, *e.g.*, Hirabayashi et al., "Novel Galactose-binding Proteins in Annelida," *J. Biol. Chem.* 273 (23): 14450-14460, 1998, provided herewith as Appendix C).

Finally, Applicants note that the ordinarily skilled artisan, upon isolating a lectin, would have no doubt as to whether that lectin is a FRIL family member based on its ability to bind to a normally glycosylated FLT3 receptor and its ability to preserve progenitor cells. Because the specification provides adequate guidance for the ordinarily skilled artisan to isolate and identify a lectin from any source as a FRIL family member, Applicants respectfully aver that undue experimentation would not be required to practice Applicants' claimed invention. Accordingly, Applicants respectfully request that this rejection under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

(ii) Claims 1-5, 9-14 and 61 stand rejected under 35 U.S.C. § 112, first paragraph, as purportedly containing subject matter which was not described in the specification in such a way

as to reasonably convey to one skilled in the relevant art that the Applicants were in possession of the claimed invention at the time the application was filed.

Applicants respectfully traverse this rejection.

As the Federal Circuit explained recently, "[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Regents of the University of California v. Eli Lilly & Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants respectfully aver that the specification not only provides a representative number of different FRIL family members, but also recites structural features common to all FRIL family members. Indeed, the claims require that each of the FRIL family members covered by the claims be able to bind to a normally glycosylated FLT3 receptor and be able to preserve progenitor cells.

Accordingly, Applicants respectfully aver that the specification has provided an adequate written description to convey to the ordinarily skilled artisan that they were in possession of the invention at the time the Application was filed. Based on these remarks, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Rejections Under 35 U.S.C.§ 102(b)

(i) Claims 1-2, 4, 9-14 and 61 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Gowda et al., J. Biol. Chem. 269: 18789-18793, 1994 (hereinafter "Gowda").

Applicants respectfully traverse this ground for rejection.

Gowda describes a mannose/glucose-specific lectin isolated from *Dolichos lab lab* (see title of Gowda).

Applicants have clarified in amended claim 1 that a FRIL family member isolated from a *Dolichos lab lab* must contain the amino acid sequence TNNVLQXT. As described in the specification (see, *e.g.*, Fig. 2), the lectin described by Gowda lacks the amino acid sequence TNNVLQXT. Gowda does not in any way teach or suggest that the lectin disclosed in their reference binds glycosylated FLT3 receptor or preserves progenitor cells, as required by Applicants' claims. Since Gowda does not teach each and every limitation of Applicants'

claimed invention it does not anticipate any of Applicants' claims (*i.e.*, claims 1-2, 4, 9-14, and 61).

Moreover, because Gowda does not describe any medical use for the lectin it describes, there is no teaching or suggestion in Gowda to combine the lectin described therein with a pharmaceutically-acceptable carrier. Failing to describe a required claim limitation, Gowda cannot anticipate claim 9 or the claims dependent thereon.

Thus, Applicants submit that this ground of rejection has been overcome. Accordingly, Applicants request that this rejection be reconsidered and withdrawn.

(ii) Claims 1-5, 9-14 and 61 stand rejected as allegedly being anticipated by Moore et al. Moore et al. do not constitute prior art under 35 U.S.C. § 102(b), as this reference was published in December 1997, which is *after* the June 24, 1997 priority date of the instant Application. Thus, this rejection has been rendered moot and should be withdrawn.

CONCLUSION

Applicants posit that the presently maintained rejections of the pending claims have been fully overcome by amendment and/or argument. Accordingly, Applicants respectfully submit that the pending claims are in condition for allowance. However, if the Examiner believes that any further discussion of this communication would be helpful, she is encouraged to contact the undersigned by telephone.

In accordance with the provisions of 37 C.F.R. §1.136(a)(1), Applicants enclose herewith a petition requesting a three month extension of time, up to and including September 22, 2003, to respond to the Office Action (September 20 being a Saturday). Please apply the three month extension of time fee to our Deposit Account No. 08-0219.

No additional fees are believed to be due in connection with this communication. However, please apply any charges, or credit any overpayment, to our Deposit Account No. 08-0219.

Respectfully submitted,

HALE AND DORR LLP

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